PATENT #10 JM 12/18/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

SCHRÖDER et al.

Serial No. 09/926,002

Filed: October 30, 2001

For: VACCINE FORMULATION

Group Art Unit: 1645

Examiner: FORD

REQUEST FOR RECONSIDERATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the Official Action of August 13, 2002, in connection with the above-identified application. The period for response has been extended to expire on December 13, 2002, by the filing herewith of a petition for a one month extension of time and payment of the required fee.

The undersigned attorney appreciates the telephone conversations with Examiner Ford at which time the possibility of a personal interview with the Examiner to discuss the outstanding rejection was discussed. The Examiner indicated that her supervisor would need to be present at the interview and it was determine that it would be better to wait until early January to conducted the interview in this application and the related '001 application. During the telephone conversation, the Examiner indicated that she was going to maintain the prior art rejection in the '001 application. The only issue in the present case is the patentability of the claimed invention over the prior art and the interview will be most helpful to consider this issue and hopefully advance the prosecution to an early allowance. The Examiner is invited to contact the undersigned attorney to make the necessary arrangements for the interview at the Examiner's convenience.

All of the claims in the present application have been rejection over the prior art as prima facie obvious. In the previous response, Applicants noted the requirements

for establishing a prima facie case of obviousness. It is believe that it is worth repeating these requirements taking into consideration the points raided in the Official Action.

Applicants again wish to note the basic requirements of a prima facie case of obviousness as set forth in the MPEP § 2143. This section states that to establish a prima facie case of obviousness, three basic criteria first must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Section 2143.03 states that all claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence present by applicant and the citation of In re Soni for error in not considering evidence presented in the specification.

The rejection of claims 11-15 under 35 U.S.C. 103(a) as being unpatentable over Schroder in view of Svenson for reasons of record has been carefully considered but is most respectfully traversed.

In the Official Action it is urged that limitations such as "mucosa administration" is being viewed as a limitation of "intended use" and that limitations such as "packaging the vaccine are as an aerosol, spray or nose drop package" is being viewed as a limitation of "design choice". Clarification on the meanings of these expressions in the

next Official Action is requested since claim limitations cannot be ignored but must be taken into consideration in determining the patentability of the claimed invention. It is assumed that all the claim limitations set forth in Applicants' claims have been considered and given full weight regardless the Examiner's characterization of these limitations.

It is urged in the Official Action that it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to add the monoglyceride preparation as taught by Schroder to the vaccine composition comprising of consisting of active carbohydrate moieties (ACM) of Svenson because Schroder et al. teach that a combination between any monogylceride and a fatty acid can stimulate the immune system and to produce antibodies and induce protective immunity. It is further concluded that it would have been expected barring evidence to the contrary, that the addition of monogylcerides to compositions consisting of carbohydrate moieties (ACM) would provide enhanced immunogenicity of antigens and the use of monogylcerides in vaccines are stable, cheaper and easy to formulate. This conclusion is specifically traversed since the references do not suggest a claim limitation which cannot be ignored.

As Applicants previously argued and as recognized in the Official Action, the claims are not directed to any vaccine formulation but to a vaccine formulation against Mycobacterium and contain limitations of an immunogenic product consisting of antigenically active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis*. Therefore, when the Examiner states on page 4 of the Official Action that the claims are directed to a vaccine formulation, this statement is incomplete in that it ignores the claim limitation with respect to *M. tuberculosis*. This is contrary to the requirements for establishing a prima facie case of obvious as set forth in the MPEP and as discussed above. It is recognized that Schroder does not teach this in the Official Action and there is no reference to this claim limitation in Svenson. Clearly, a prima facie case of obviousness cannot be established when the prior art does not specify or suggest claim limitations. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103(a) as being unpatentable over Schroder in view of Svenson and further in view of Vercellone et al. has been carefully considered but is most respectfully traversed.

Applicants note the Examiner's comments with respect to the teachings of Vercellone and note the conclusion that it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to further modify the vaccine composition as combined supra according to the teaching of Vercellone et al. because Vercellone et al. teaches that lipoarabinomannan has the ability to insert into membranes without the involvement of any receptor and that lipoarabinomannan stimulates double negative T cells which contributes to the protective immunity against tuberculosis. Applicants note that Vercellone et al. describes production of LAM (lipoarabinomannan), i.e., a carbohydrate moiety, derived form *Mycobacterium tuberculosis* as well as its stimulation of TNF-alpha and cytokines. There is no mention of the use of LAM for the production of a vaccine against Tuberculosis neither is there any mention of the suitability of covalently linking LAM to a specific linker that also is bound to an immunoactivating carrier. Furthermore, Vercellone et al. does not describe a method for vaccinating an animal against a mycobacterium.

Applicants most respectfully submit that one of ordinary skill in the art would have no reason to combine the teachings of Schroder and/or Svenson when developing a TB vaccine as none of these documents mention a TB vaccine. Furthermore, a person skilled in the art would have no reason to combine the teachings of Schroder and/or Svenson with the teaching of Vercellone et al. as Vercellone et al. do not describe any specific vaccine absent the teaching in Applicants' specification. In re Fritch, 23 USPQ 1780, 1784(Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.). Moreover, obvious to try is not the standard of obviousness under 35 USC 103(a). Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 11-37 under 35 U.S.C. 103(a) as being unpatentable over Schroder, Svenson and Vercellone et al. and in further view of Hansen et al. has been

carefully considered but is most respectfully traversed for the above reasons and that the teachings of the Hansen et al reference does not overcome the deficiencies of the primary references. The Hansen et al reference relates to fat emulsion for intravenous administration and describes a 10% soybean emulsion . Controlled studies have shown that the soybean oil emulsion can be substituted for glucose to supply one-third to two-thirds of the total calories. It is not seen who this reference overcomes the deficiencies of the prima references as discussed above. Why would one skilled in the art add soybean oil emulsion described for caloric intake into a vaccine, absent, Applicants teaching which may not be used to establish a prima facie case of obviousness. Clearly, this teaching does not overcome the deficiencies of the previous teachings and does not establish the obviousness of the claimed invention. Contrary to the assertion in the Official Action, Applicants arguments are fully commensurate with the claimed invention. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 38-42 under 35 U.S.C. 103(a) as being unpatentable over Reed et al. in view of Schroder and in further view of Svenson has been carefully considered but is most respectfully traversed. In summary, Applicants wish to point out that the teachings of the reference most be considered as whole as would be appreciated by one of ordinary skill in the art. One skilled in the art would not ignore important aspects of the invention as described in the reference and only pick and choose specific aspects to arrive at the presently claimed invention.

Applicants most respectfully direct the summary of the invention described in the Reed et al patent which states that this invention provides compositions and methods for preventing and treating M. tuberculosis infection. In one aspect, pharmaceutical compositions are provided that comprise a physiologically acceptable carrier and either (a) a first polypeptide and a second polypeptide, or (b) a fusion protein including a first polypeptide and a second polypeptide, wherein each of the polypeptides comprises an immunogenic portion of a M. tuberculosis antigen or a variant thereof. In specific embodiments, the first polypeptide comprises an immunogenic portion of a M. tuberculosis antigen having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 91, 107, 109, 111 and variants thereof, and the

second polypeptide comprises an immunogenic portion of a M. tuberculosis antigen having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 79, 88, 115, 117, 118, 119 and variants thereof. Why would one of ordinary skill in the art avoid these clear teachings and try to combine this reference with Svenson with a reasonable expectation of obtaining the presently claimed invention?

The Reed et al invention also provides vaccines comprising an immune response enhancer and either (a) a first polypeptide and a second polypeptide, or (b) a fusion protein including a first polypeptide and a second polypeptide, wherein each of the polypeptides comprises an immunogenic portion of a M. tuberculosis antigen or a variant thereof. In specific embodiments, the first polypeptide comprises an immunogenic portion of a M. tuberculosis antigen having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 91, 107, 109, 111 and variants thereof, and the second polypeptide comprises an immunogenic portion of a M. tuberculosis antigen having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 79, 88, 115, 117, 118, 119 and variants thereof. There is no motivation to combine the teachings of Svenson with Reed et al absent Applicants' specification.

Applicants note that in preferred embodiments, the immune response enhancer employed in the inventive vaccines is an adjuvant. Most preferably, the adjuvant comprises 3-de-O-acylated monophosphoryl lipid A (3D-MPL) or the saponin QS21, or a combination of both 3D-MPL and QS21. The vaccines of Reed et al may also, or alternatively, comprise an immunostimulatory cytokine or chemokine. Preferably, the vaccines are formulated in an oil in water emulsion. This teaching even with Schroder teaches no more than obvious to try which is not the standard of obviousness under 35 USC 103(a) and in no way leads one of ordinary skill in the art to the teachings of Svenson. Why would one of ordinary skill modify the specific vaccines of Reed et al with the teaching of Svenson? There is none other than the impermissible use of Applicants' teaching. Clearly, Applicants' specification is being used as a template to

arrive at the claimed invention from the prior art. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 38-45 under 35 U.S.C. 103(a) as being unpatentable over Reed et al., Schroder, Svenson and further in view of Vercellone et al. has been carefully considered but is most respectfully traversed for the reasons discussed above with respect to the primary references.

Applicants have previously noted that Vercellone et al. describes production of LAM (lipoarabinomannan), i.e., a carbohydrate moiety, derived form *Mycobacterium tuberculosis* as well as its stimulation of TNF-alpha and cytokines. There is no mention of the use of LAM for the production of a vaccine against Tuberculosis neither is there any mention of the suitability of covalently linking LAM to a specific linker that also is bound to an immunoactivating carrier. Furthermore, Vercellone et al. does not describe a method for vaccinating an animal against a mycobacterium.

Applicants most respectfully submit that one of ordinary skill in the art would have no reason to combine the teachings of Schroder and/or Svenson when developing a TB vaccine as none of these documents mention a TB vaccine. Furthermore, a person skilled in the art would have no reason to combine the teachings of Schroder and/or Svenson with the teaching of Vercellone et al. as Vercellone et al. do not describe any specific vaccine absent the teaching in Applicants' specification. Applicants most respectfully submit that Schroder relates to a novel adjuvant for use in vaccine compositions. The adjuvant is a mixture of a monoglyceride preparation and fatty acid. In Schroder, the only antigens mentioned are diphtheria toroid, influenza virus, and rotavirus. In re Fritch, 23 USPQ 1780, 1784(Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.). Moreover, obvious to try is not the standard of obviousness under 35 USC 103(a).

Svenson relates to the use of a conjugate wherein an antigenically active carbohydrate moiety (ACM) is covalently coupled via a divalent bridge group to immunologically active carriers (IAC). Specific examples of ACM given in the citation

are saccharides from Salmonella, Streptococcus pneumonia and Haemophilus influenza. The inclusion of the teachings of the Reed et al reference, while admittedly directed to tuberculosis, did not teach the type of vaccine as presently claimed and the combination does not describe the claimed invention. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 38-46 under 35 U.S.C. 103(a) as being unpatentable over Reed, et al., Schroder, Svenson, Vercellone et al. and further in view of Hansen et al. has been carefully considered but is most respectfully traversed for the above reasons and that the teachings of the Hansen et al reference does not overcome the deficiencies of the primary references. The Hansen et al reference relates to fat emulsion for intravenous administration and describes a 10% soybean emulsion . Controlled studies have shown that the soybean oil emulsion can be substituted for glucose to supply one-third to two-thirds of the total calories. It is not seen how this reference overcomes the deficiencies of the prima references as discussed above. Why would one skilled in the art add soybean oil emulsion described for caloric intake into a vaccine, absent, Applicants teaching which may not be used to establish a prima facie case of obviousness. Clearly, this teaching does not overcome the deficiencies of the previous teachings and does not establish the obviousness of the claimed invention. Contrary to the assertion in the Official Action, Applicants arguments are fully commensurate with the claimed invention. Accordingly, it is most respectfully requested that this rejection be withdrawn.

In view of the above comments, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,
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DATE: December 13, 2002